Point Estimates of Transfusion Risk from Quantitative Models of Deferral Policy Changes

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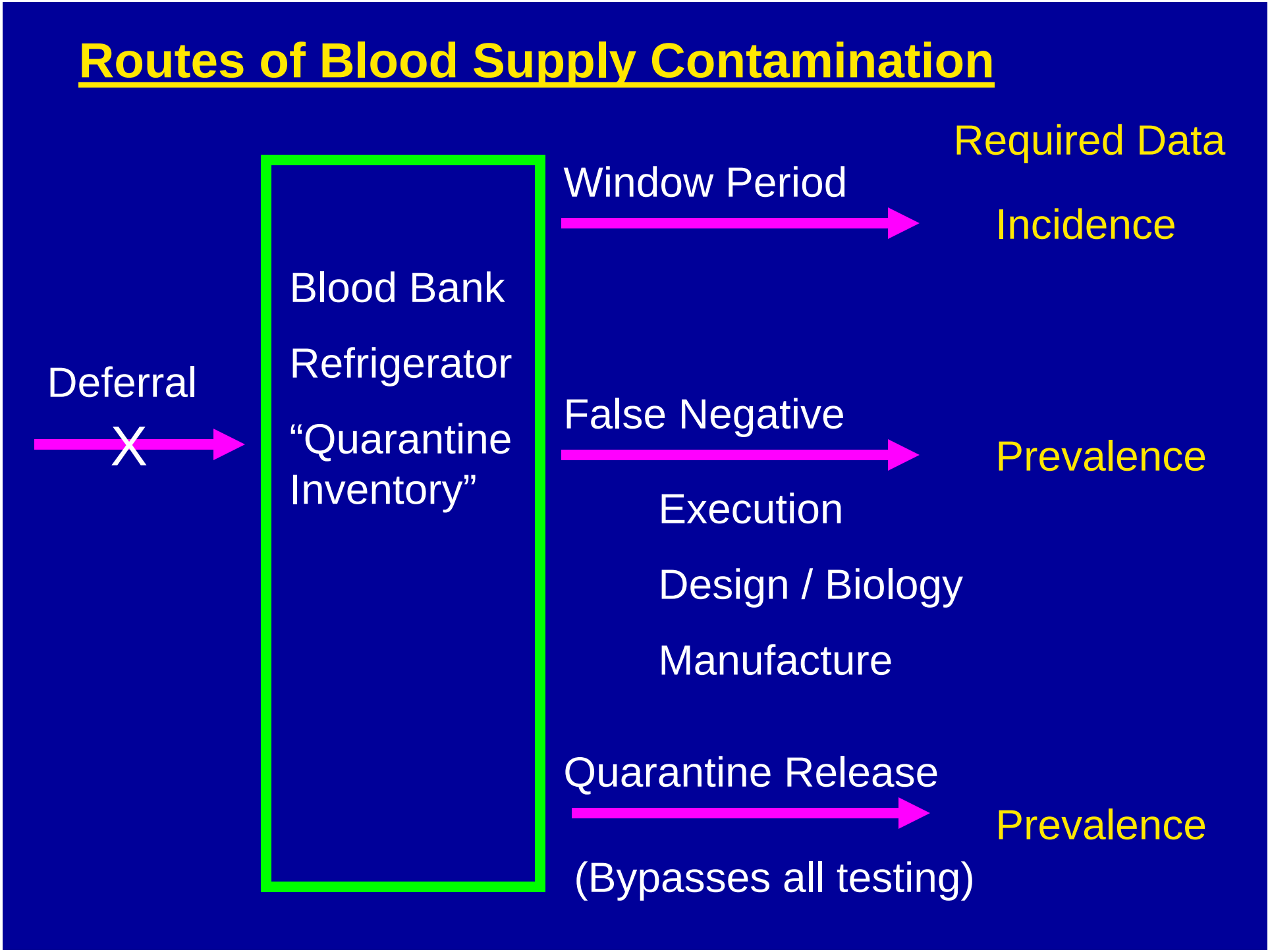
- History
- General Approaches – general population and blood donor issues.
- Changes in risk w.r.t. changes in policy as opposed to total risk.

Routes of Blood Supply Contamination



Quantification of Infectious Donations Entering the Blood Supply as a Function of Changes in Deferral Policy I

- Change in risk as a function of change in the size of the donor pool with the specific characteristics being modeled.

1. Change in the size of the donor pool (the “quarantine inventory” term.)
2. Prevalence and incidence terms times the “quarantine inventory” term = the number of infectious donations that enter quarantine.
3. False Negative & Quarantine Release (separately) times the number of infectious “prevalence” donations in quarantine = the actual number of infectious “prevalence”donations to escape interdiction .

Quantification of Infectious Donations Entering the Blood Supply as a Function of Changes in Deferral Policy: Calculation of Change

$$\Delta EWP + \Delta EFN + \Delta EQR = \Delta E \text{ (total errors)}$$

Estimation of Change in Quarantine Inventory

- As an illustrative example, consider changing donor suitability criteria to defer for MSM behavior within the last 5 years prior to donation, or within the last 1 year.

Estimation of the quarantine inventory term for MSM: What increments in quarantined MSM units would result from a switch to a 5 or 1 year deferral policy for MSM?*

- Yearly donation rate = 5%.
- ~16% of potential new donors are probably already donating

Years Abstention	New Donors Eligible	New Donations (Potential)	New Donations (Potential – Current)
5	1.7 million	85,000	71,400
1	3.3 million	165,000	139,000

*Extrapolated from data from National Center for Health Statistics and/or REDS

Estimation of the quarantine inventory term for **IDU**

Years Abstention	New Donors Eligible	New Donations (Potential)	New Donations (Potential – Current)
1	2.3 million	116,000	92,500*

*2003 National Survey on Drug Use and Health (NSDUH),

HIV Prevalence in MSM

“non-MSM” General population	MSM	Ratio: MSM / general
0.14%	8%	~60

Effective HIV Prevalence in Donors

- 75% of HIV infected MSM know their serostatus.
- Likely MSM donors = ~2% based on self deferral.

	HIV Prevalence Current Donors*	Ratio: MSM (2%) / current
First Time Donors	1 / 10,000	200
Repeat Donors	0.1 / 10,000	2000

*ARC

Calculation of Infectious Units Entering Quarantine Inventory

- For 5 yr deferral: 2% of 71,400 = 1430
- For 1 yr deferral: 2% of 139,000 = 2780

These are non-window period infectious sources for blood supply contamination.

Window Period (WP) Issues

- Window Period = time from infection to detectability
- Delayed seroconversion in the NAT Era
- For HIV, HCV, HBV and HTLV window periods greater than 1 year are extremely rare.
- The deferral policies generally being considered for high risk behavior are for 1 year or more.

Window Period (WP) Issues - Conclusion

$\Delta EWP = 0$

$\Delta E = \Delta EFN + \Delta EQR$

“False Negative” Rates

Unspecified execution errors

Defective test kit

} Measured by Re-testing

Design / Biology

Data from PIs

Clinical Course of Infection

“False Negative” Rates: Measured in Blood Environment

Measured by Re-testing*

HCV		HIV	
EIA	NAT	EIA	NAT
3/10,000**	5/10,000***	<17/10,000$	<17/10,000$

* Michael Busch, UCSF

** actual data: 4/13,662

*** actual data: 1/2136 - extrapolated

$ actual data: 0 / 580

HIV & HCV “False Negatives”: “Overlapping” Protection of EIA & NAT

	EIA	NAT	Simultaneous Error Rate
HIV	17 / 10,000	17 / 10,000	0.03 / 10,000

MSM / HIV:
Yearly HIV Donations Entering the Blood Supply as a Result of "False Negative" Test Results

5 yr Deferral: ΔEFN = 3 / 1 million X 1430 = 0.004

1 yr Deferral: ΔEFN = 3 / 1 million X 2780 = 0.008

HCV “FN” Rate

EIA (Test Error)	NAT (Biological Error)	Simultaneous Error Rate
3 / 10,000*	2 / 10**	0.6 / 10,000

* Busch

**NHANES (’99-’02)

HBV “FN” Rate

HBsAg (Biological Error)	Anti HBc	Simultaneous Error Rate
95 / 100	3 / 10,000**	3 / 10,000

*Assuming anti-HBc has error rate equivalent to HCV EIA

HTLV “FN” Rate

- Only one assay -> no overlap protection.
- Delayed seroconverters (not modeled)

Citation	FN rate
Liu et al, 1999 *Transfusion*	5/1000
Poiesz et al, 2000 *Transfusion*	2/10
Typical *	**5/100**

*Poiesz, personal communication

Quarantine Release Errors : New York State

Facility type (# donations)	Repeat Reactive Test	Reported Incidents*	Predicted Prevalence in Quarantine Inventory**	Release Rate**
Hospitals (70,000)	Anti-HCV+	1	59	170 / 10,000
	Anti-HBV core	4	318	130 / 10,000
Blood Centers (630,000)	Anti-HCV+	0	535	0
	Anti-HBV core	1	2867	3.5 / 10,000

* Jeanne Linden, personal communication

* *Donations, based on blood bank prevalence, ARCNET (7/1/98-6/30/99)

Quarantine Release Errors: Predicted releases based on New York State Data (Jeanne Linden).

How many HIV-positive units could be inappropriately released by changing to a **1 year** MSM deferral policy?

	HIV+ (MSM x P)	Rate (Per unit)	components released*
Hospitals (6%)	167	13 / 1000	3.7
Blood Centers (94%)	2613	0.35 / 1000	1.6

*1.7 components / donation

Total 5.3

Biological Product Deviation Reports
Whole Blood: 2003 through 2005
Confirmed Positive (CP) Units Released

		Errors Reported	
Agent	Whole Blood Industry CP*	Blood Centers	Hospitals
HIV	1232	0	0
HCV	16,699	1	0
HBsAg	5935	0	0
HTLV	1270	0	0
Syphilis	12,187	1	0

*Extrapolated from ARC data, Jan 2003-September 2005

Biological Product Deviation Reports
Whole Blood: 2003 through 2005
Repeat Reactive RR (violative) units (including CP)

		Errors Reported	
Agent	Whole Blood Industry RR*	Blood Centers	Hospitals
HIV	27,433	3	1
HCV	48,525	1	2
HBsAg	24,684	0	2
HBc	131,673	3	3
HTLV	46,769	3	2
Syphilis	29,848	2	3

*Extrapolated from ARC data, Jan 2003-September 2005

Biological Product Deviation Reports: Quarantine Release Error Rates

Aggregate Data for HIV, HCV, HBV, HTLV & Syphilis

	Blood Centers	Hospitals
Confirmed Positive	0.5 / 10,000	
Repeat Reactive	0.4 / 10,000	7 / 10,000

HIV Infectious Components Predicted to Newly Enter the Blood Supply as a Result of Changing Deferral for MSM

	5 year	1 year
ΔEWP	0	0
ΔEFN	0.007	0.01
ΔEQR	0.2 – 3	0.3 – 5

Violative Risks for HIV, HBV and HCV According to Behavioral Exclusion

	Agent / Prevalence	ΔEFN donations	ΔEQR* donations	ΔE total Components**
MSM 5	HIV / 2%	0.004	0.1	0.2
	HBV / 18%-40%	3.8-8	1-2	8-18
MSM 1	HIV / 2%	0.008	0.2	0.3
	HBV / 18%-40%	7.5-16	2-4	16-35
IDU 1	HIV / 5.9%	0.02	0.36	0.6
	HBV / 23%-60%	6-17	1.4-3.7	13-35
	HCV / 58%	3	3.6	12
	HTLV / 10%	460	1	780

•Based on BPDR only **components = 1.9 X donations

Conclusions: Infectious Risk vs Current Risk

HBV infectious ~ 0.05 X violative; HCV infectious ~ 0.8 X violative

Behavior	Agent	ΔE* BPDR	ΔE* NY Data	Current Yearly*
MSM 5yr	HIV	0.2	3	12
	HBV	0.4-0.9	1.4-3.2	85
MSM 1 yr	HIV	0.3	5	12
	HBV	0.8-1.7	3-6	85
IDU 1 yr	HIV	0.6	9	12
	HBV	0.7-1.7	2.4-6	85
	HCV	9	80	12
	HTLV	780	800	36

*Infectious Components

Conclusions:
Infectious Risk as % of Current Risk

HBV infectious ~ 0.05 X violative; HCV infectious ~ 0.8 X violative

Behavior	Agent	ΔE* BPDR%	ΔE* NY Data%
MSM 5yr	HIV	1.7	25
	HBV	0.5-1	1.6-3.8
MSM 1 yr	HIV	2.5	40
	HBV	0.9-2	3.5-7
IDU 1 yr	HIV	5	75
	HBV	0.8-2	2.8-7
	HCV	75	670
	HTLV	2100	2200

*Infectious Components

- Prevalence invariant w.r.t. abstinence
- Effective prevalence
- NY data suggests caution (HIV/MSM)
- IDU dangerous (HCV & HTLV)

Needs for Future Research

1. Prevalence in identifiable behavioral categories, particularly prevalence w.r.t. abstention.
2. Self knowledge of serostatus.
3. FN rates (HBV, HTLV), particularly in Hospitals
4. Quarantine Release Errors (hospital quarantine prevalence rates of infectious agents).